JEM

THE
JOURNAL OF
EXPERIMENTAL
MEDICINE

VOLUME 202 NUMBER 1
JULY 4, 2005
www.jem.org

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ON THE COVER
**Graphic art by New York artist Dan Durso (durso10@yahoo.com) representing expression of tissue-restricted antigens by medullary thymic epithelial cells, which increases progressively as the cells differentiate. See related article by Derbinski et al. (page 33) and commentary by Gillard and Farr (page 15).**

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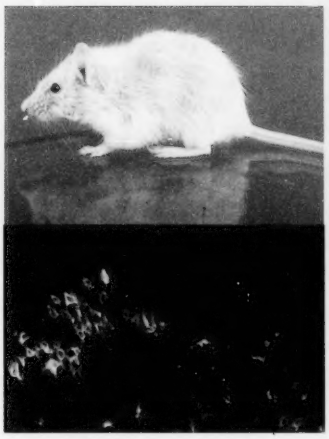

**Mice with a limited MHC–peptide repertoire spontaneously develop autoimmune dermatitis mediated by $CD8^+$ T cells (yellow).**
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**Production of interferon-α by skin-infiltrating plasmacytoid DCs (yellow) activates T cells (blue) and triggers psoriasis.**
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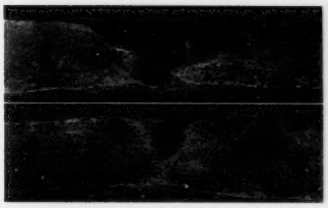

**Inactivation of the transcription factor NF-κB (bottom) improves recovery and reduces lesion size (red) after spinal cord injury.**
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ON THE COVER
**Painting by New York artist Emilie Clark (emilie@sharkbooks.com) representing the characteristic gold color of *Staphylococcus aureus*, which allows the bacteria to evade host immune defenses. Related article by Liu et al.**
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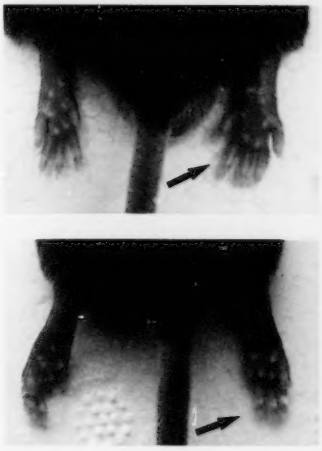

**The neuropeptide neuromedin U (NMU) is required for mast cell activation and footpad swelling in response to local inflammation (wild-type, top; *NMU*$^{-/-}$, bottom).**
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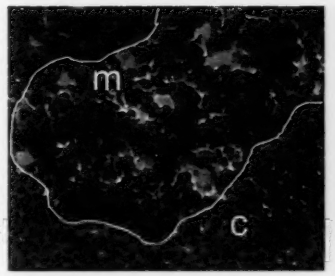


**CD1d (red) expressed on cortical thymocytes, but not MHC class II$^+$ cells (green), is necessary and sufficient for NKT cell development and survival.**
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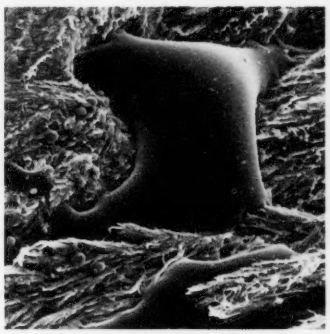

ON THE COVER
**Image shows a colored scanning EM of a multinucleated osteoclast (purple) surrounded by bone (brown). In mice lacking the receptor DC-STAMP, osteoclasts cannot fuse, resulting in poor bone resorption and increased bone mass (osteopetrosis). Image provided by David Scharf, Photo Researchers, Inc. Related article by Yagi et al.**
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379 **Adoptive transfer of cytomegalovirus-specific CTL to stem cell transplant patients after selection by HLA–peptide tetramers**
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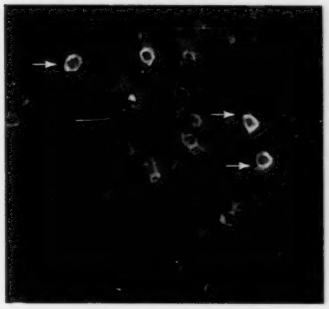
445 **Selective targeting of regulatory T cells with CD28 superagonists allows effective therapy of experimental autoimmune encephalomyelitis**
Niklas Beyersdorf, Stefanie Gaupp, Karen Balbach, Jens Schmidt, Klaus V. Toyka, Chia-Huey Lin, Thomas Hanke, Thomas Hünig, Thomas Kerkau, and Ralf Gold



**Effective priming of herpes simplex virus–specific CD8$^+$ cells by lymph node dendritic cells (DCs; red) requires contact between lymph node DCs and plasmacytoid DCs (yellow) in the draining lymph node.**
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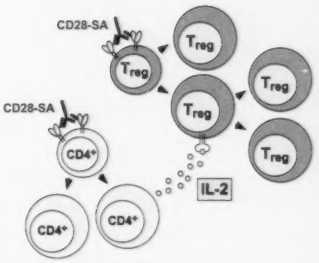


**A CD28 superagonist induces preferential expansion of CD4$^+$CD25$^+$ regulatory T cells and protects rats against experimental autoimmune encephalomyelitis.**
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THE JOURNAL OF EXPERIMENTAL MEDICINE
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485 Characterization of the early stages of thymic NKT cell development
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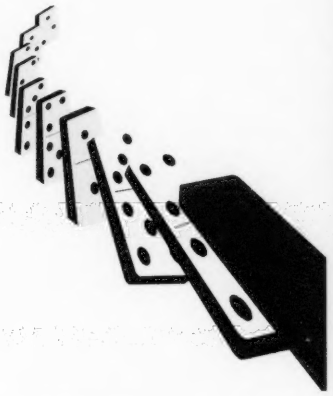

ON THE COVER
Linear groups of T cell receptors (TCRs), but not single TCRs, respond to low doses of antigen. Activation-induced phosphorylation of one TCR might facilitate phosphorylation of the neighboring TCR, creating a domino-like effect and maximizing an otherwise weak signal. Graphic art by New York artist Dan Durso (durso10@yahoo.com). Related article by Schamel et al.
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493 **Coexistence of multivalent and monovalent TCRs explains high sensitivity and wide range of response**
Wolfgang W.A. Schamel, Ignacio Arechaga, Ruth M. Risueño, Hisse M. van Santen, Pilar Cabezas, Cristina Risco, José M. Valpuesta, and Balbino Alarcón
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505 **XBP-1 specifically promotes IgM synthesis and secretion, but is dispensable for degradation of glycoproteins in primary B cells**
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517 **11β-HSD1 inhibition ameliorates metabolic syndrome and prevents progression of atherosclerosis in mice**
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529 **Microsomal triglyceride transfer protein lipidation and control of CD1d on antigen-presenting cells**
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541 **Spontaneous atopic dermatitis in mice expressing an inducible thymic stromal lymphopoietin transgene specifically in the skin**
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551 **IL-4 receptor expression on $CD8^+$ T cells is required for the development of protective memory responses against liver stages of malaria parasites**
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561 **Inducible DNA breaks in Ig S regions are dependent on AID and UNG**
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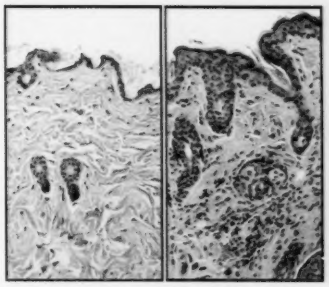

**Expression of the cytokine thymic stromal lymphopoietin in keratinocytes causes increased T helper 2 responses and an atopic dermatitis–like condition in mice (right).**
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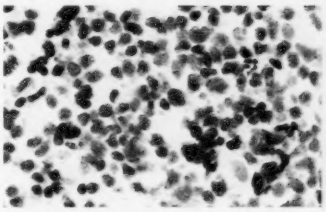

**Lymph node from a patient with common variable immunodeficiency and granulomatous/lymphocytic interstitial lung disease showing presence of human herpesvirus 8 proteins (brown).**
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JEM

THE JOURNAL OF EXPERIMENTAL MEDICINE

VOLUME 202 NUMBER 5
SEPTEMBER 5, 2005
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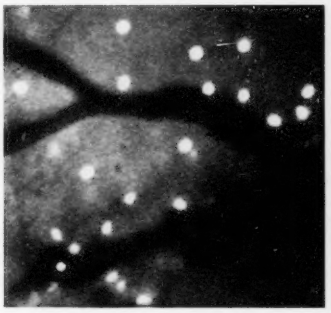

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**False color intravital microscopy image of interferon-producing cells (yellow) migrating out of high endothelial venules (purple) into peripheral lymph nodes in response to an inflammatory stimulus. Related article by Diacovo et al.**
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697 **Unexpected prolonged presentation of influenza antigens promotes CD4 T cell memory generation**
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707 **Protein phosphatase subunit G5PR is needed for inhibition of B cell receptor–induced apoptosis**
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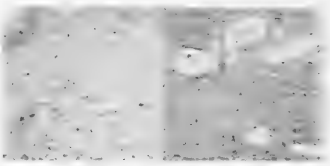
721 **Correction**



**Tumor tissue (right) from patients with tuberous sclerosis complex contains increased numbers of $CD68^+$ cells (brown) due to the increased production of the chemokine MCP-1.**
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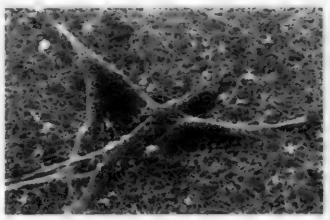

**Scanning electron micrograph showing vascular smooth muscle cells migrating in a collagen matrix, a process that requires mobilization of the metallo-protease MT1-MMP.**
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751 The structure of human CD23 and its interactions with IgE and CD21
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761 Divergent roles of IL-23 and IL-12 in host defense against *Klebsiella pneumoniae*
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783 **Expression of the immunoregulatory molecule FcRH4 defines a distinctive tissue-based population of memory B cells**
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817 **Chloroquine enhances human $CD8^+$ T cell responses against soluble antigens in vivo**
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841 **Cytosolic phospholipase $A_2\alpha$–deficient mice are resistant to experimental autoimmune encephalomyelitis**
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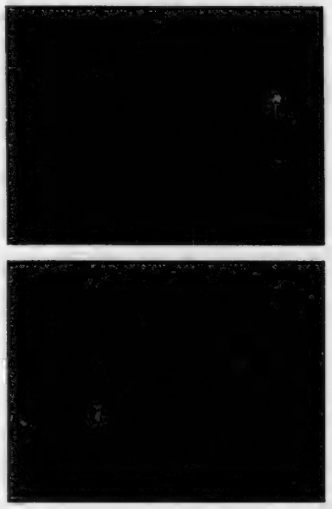
865 **Eosinophil adhesion under flow conditions activates mechanosensitive signaling pathways in human endothelial cells**
Susan L. Cuvelier, Smitha Paul, Neda Shariat, Pina Colarusso, and Kamala D. Patel

877 **Correction**

879 **Correction**



**Autoimmune T cell (red) attack on the ovaries (top) is prevented by antigen-dependent regulatory T cells (bottom).**
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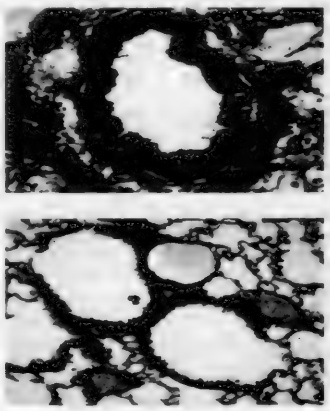

**Lung inflammation (top) in response to an inhaled allergen is absent in mice lacking the cytokine TSLP (bottom).**
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907 Removal of homeostatic cytokine sinks by lymphodepletion enhances the efficacy of adoptively transferred tumor-specific CD8$^+$ T cells
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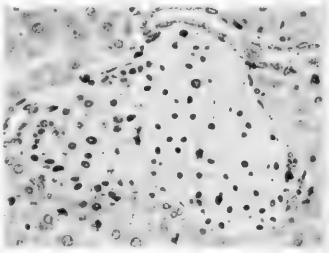

ON THE COVER
Image shows interferon-γ–producing neutrophils (brown) infiltrating transplanted pancreatic islet cells. NKT cells activate the neutrophils, and both cell types contribute to early islet cell rejection. Related article by Yasunami et al.
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919 **Tumor cells convert immature myeloid dendritic cells into TGF-β–secreting cells inducing $CD4^+CD25^+$ regulatory T cell proliferation**
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941 **IL-18–induced $CD83^+CCR7^+$ NK helper cells**
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955 **TIM-2 is expressed on B cells and in liver and kidney and is a receptor for H-ferritin endocytosis**
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967 **FASL –844C polymorphism is associated with increased activation-induced T cell death and risk of cervical cancer**
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975 **Lysophosphatidic acid inhibits cholera toxin-induced secretory diarrhea through CFTR-dependent protein interactions**
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987 **The human macrophage mannose receptor directs *Mycobacterium tuberculosis* lipoarabinomannan-mediated phagosome biogenesis**
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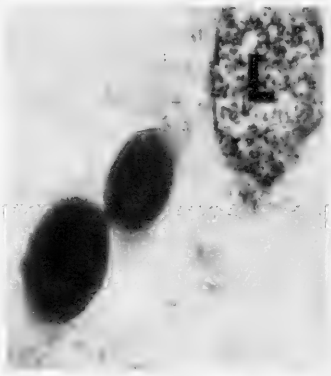
1001 **Cytolytic granule polarization and degranulation controlled by different receptors in resting NK cells**
Yenan T. Bryceson, Michael E. March, Domingo F. Barber, Hans-Gustaf Ljunggren, and Eric O. Long


**Phagosomes containing beads coated with *Mycobacterium tuberculosis* mannose-capped lipoarabinomannan (black) fail to fuse with neighboring lysosomes (L).**
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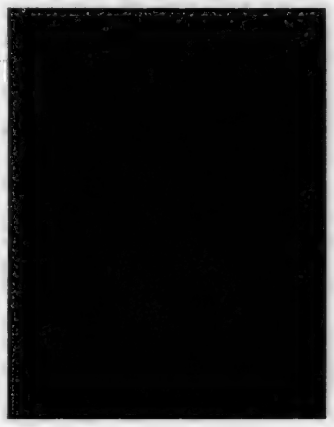

**FoxP3-expressing regulatory T cells (green) are localized in the thymic medulla (red) during development.**
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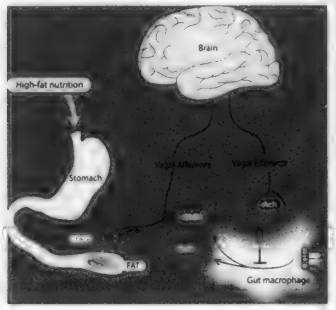


ON THE COVER
**The diagram depicts the activation of the cholinergic antiinflammatory pathway by dietary fat. Related article by Luyer et al.**
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1031 Actin and agonist MHC–peptide complex–dependent T cell receptor microclusters as scaffolds for signaling
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1037 Notch signaling is an important regulator of type 2 immunity
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1043 Innate immunity against *Francisella tularensis* is dependent on the ASC/caspase-1 axis
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1063 Functional specialization of gut CD103$^+$ dendritic cells in the regulation of tissue-selective T cell homing
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1075 $CD4^+CD25^+$ regulatory T cells inhibit natural killer cell functions in a transforming growth factor–β–dependent manner
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1087 Chemokine receptor CCR5 promotes leukocyte trafficking to the brain and survival in West Nile virus infection
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1099 SOCS-1 regulates IL-15–driven homeostatic proliferation of antigen-naive CD8 T cells, limiting their autoimmune potential
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1109 Endogenous human cytomegalovirus gB is presented efficiently by MHC class II molecules to $CD4^+$ CTL
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1121 Deletion of DOCK2, a regulator of the actin cytoskeleton in lymphocytes, suppresses cardiac allograft rejection
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1131 Nucleic acids of mammalian origin can act as endogenous ligands for Toll-like receptors and may promote systemic lupus erythematosus
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1141 The *Scurfy* mutation of *FoxP3* in the thymus stroma leads to defective thymopoiesis
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$CD103^+$ dendritic cells (yellow) induce the expression of the gut-homing chemokine receptor CCR9 on $CD8^+$ T cells.
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1179 Live attenuated yellow fever 17D infects human DCs and allows for presentation of endogenous and recombinant T cell epitopes
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1185 A role for dual viral hits in causation of subacute sclerosing panencephalitis
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1191 The insulin A-chain epitope recognized by human T cells is posttranslationally modified
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1199 Suppression of allergic airway inflammation by helminth-induced regulatory T cells
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**The image is a photograph of the intestinal helminth *Heligmosomoides polygyrus*. Infections with *H. polygyrus* induce regulatory T cells that inhibit subsequent responses to inhaled allergens. Photograph by Constance Finney. Related article by Wilson et al.**
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1213 **TSLP-activated dendritic cells induce an inflammatory T helper type 2 cell response through OX40 ligand**
Tomoki Ito, Yui-Hsi Wang, Omar Duramad, Toshiyuki Hori, Guy J. Delespesse, Norihiko Watanabe, F. Xiao-Feng Qin, Zhengbin Yao, Wei Cao, and Yong-Jun Liu

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1235 **Interaction of CagA with Crk plays an important role in *Helicobacter pylori*–induced loss of gastric epithelial cell adhesion**
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1249 **The immunogenicity of a viral cytotoxic T cell epitope is controlled by its MHC-bound conformation**
Fleur E. Tynan, Diah Elhassen, Anthony W. Purcell, Jacqueline M. Burrows, Natalie A. Borg, John J. Miles, Nicholas A. Williamson, Kate J. Green, Judy Tellam, Lars Kjer-Nielsen, James McCluskey, Jamie Rossjohn, and Scott R. Burrows

1261 **Autoamplification of NFATc1 expression determines its essential role in bone homeostasis**
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1271 **CD4 T cells integrate signals delivered during successive DC encounters in vivo**
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1279 **Differential antitumor immunity mediated by NKT cell subsets in vivo**
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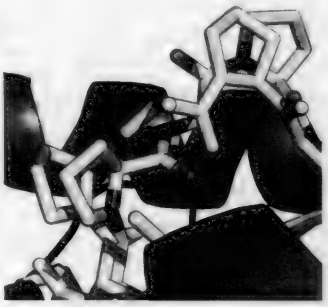
1289 **IL-2 production in developing Th1 cells is regulated by heterodimerization of RelA and T-bet and requires T-bet serine residue 508**
Eun Sook Hwang, Jeong-Ho Hong, and Laurie H. Glimcher

1301 **Correction**



**A CD8$^+$ T cell epitope from EBV adopts different conformations when bound to HLA-B*3508 (peptide in yellow) and HLA-B*3501 (peptide in grey).**
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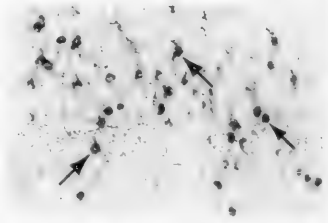

**Measles virus (brown) infects neurons in a mouse model of the fatal neurodegenerative disease subacute sclerosing panencephalitis.**
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1319 *Schistosoma mansoni* secretes a chemokine binding protein with antiinflammatory activity
Philip Smith, Rosie E. Fallon, Niamh E. Mangan, Caitriona M. Walsh, Margarida Saraiva, Jon R. Sayers, Andrew N.J. McKenzie, Antonio Alcami, and Padraic G. Fallon
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1327 *Yersinia* virulence factor YopJ acts as a deubiquitinase to inhibit NF-κB activation
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1333 Toll-like receptor–independent gene induction program activated by mammalian DNA escaped from apoptotic DNA degradation
Yasutaka Okabe, Kohki Kawane, Shizuo Akira, Tadatsugu Taniguchi, and Shigekazu Nagata
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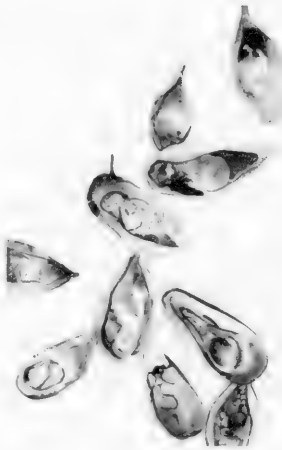

ON THE COVER
Painting by New York artist Emilie Clark (emilie@sharkbooks.com) showing *Schistosoma mansoni* eggs. These parasite eggs secrete a chemokine binding protein thereby suppressing the inflammatory response. Related article by Smith et al.
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1341 **Gadd45β and Gadd45γ are critical for regulating autoimmunity**
Lin Liu, Elise Tran, Yani Zhao, Yuchen Huang, Richard Flavell, and Binfeng Lu
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1349 **Avidity for antigen shapes clonal dominance in CD8$^+$ T cell populations specific for persistent DNA viruses**
David A. Price, Jason M. Brenchley, Laura E. Ruff, Michael R. Betts, Brenna J. Hill, Mario Roederer, Richard A. Koup, Steven A. Migueles, Emma Gostick, Linda Wooldridge, Andrew K. Sewell, Mark Connors, and Daniel C. Douek

1363 **BAFF regulates B cell survival by downregulating the BH3-only family member Bim via the ERK pathway**
Andrew Craxton, Kevin E. Draves, Adriana Gruppi, and Edward A. Clark

1375 **Sequential development of interleukin 2–dependent effector and regulatory T cells in response to endogenous systemic antigen**
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1387 **Where CD4$^+$CD25$^+$ T reg cells impinge on autoimmune diabetes**
Zhibin Chen, Ann E. Herman, Michael Matos, Diane Mathis, and Christophe Benoist

1399 **Coordinated oncogenic transformation and inhibition of host immune responses by the PAX3-FKHR fusion oncoprotein**
Stephen Nabarro, Nourredine Himoudi, Antigoni Papanastasiou, Kimberly Gilmour, Sian Gibson, Neil Sebire, Adrian Thrasher, Michael P Blundell, Mike Hubank, Glenda Canderan, and John Anderson
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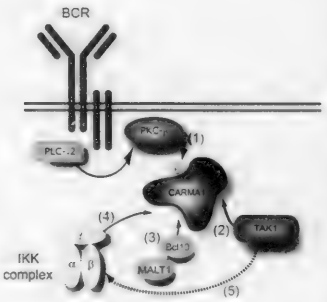
1411 **PU.1 is not strictly required for B cell development and its absence induces a B-2 to B-1 cell switch**
Min Ye, Olga Ermakova, and Thomas Graf

1423 **PKCβ regulates BCR-mediated IKK activation by facilitating the interaction between TAK1 and CARMA1**
Hisaaki Shinohara, Tomoharu Yasuda, Yuichi Aiba, Hideki Sanjo, Megumi Hamadate, Hiroshi Watarai, Hiroaki Sakurai, and Tomohiro Kurosaki

1433 **Selective accumulation of differentiated CD8$^+$ T cells specific for respiratory viruses in the human lung**
Godelieve J. de Bree, Ester M.M. van Leeuwen, Theo A. Out, Henk M. Jansen, René E. Jonkers, and René A.W. van Lier

1443 **The very 5′ end and the constant region of Ig genes are spared from somatic mutation because AID does not access these regions**
Simonne Longerich, Atsushi Tanaka, Grazyna Bozek, Dan Nicolae, and Ursula Storb




**Activation of NF-κB in response to B cell receptor ligation requires phosphorylation of the adaptor molecule CARMA1 by protein kinase C-β.**
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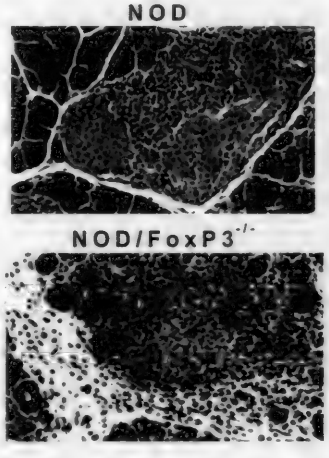


**T cells (small purple dots) that invade pancreatic islet cells are more aggressive in NOD mice that lack regulatory T cells (NOD/FoxP3$^{-/-}$).**
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Suppressive CpG
No entry for adenosine
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1465 Autoantibodies make a U-turn: the toll hypothesis for autoantibody specificity
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1471 Blimp-1 is required for maintenance of long-lived plasma cells in the bone marrow
Miriam Shapiro-Shelef, Kuo-I Lin, David Savitsky, Jerry Liao, and Kathryn Calame

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1477 Adenovirus serotype 5 E1A sensitizes tumor cells to NKG2D-dependent NK cell lysis and tumor rejection
John M. Routes, Sharon Ryan, Kristin Morris, Rayna Takaki, Adelheid Cerwenka, and Lewis L. Lanier

1483 Endomucin, a CD34-like sialomucin, marks hematopoietic stem cells throughout development
Azusa Matsubara, Atsushi Iwama, Satoshi Yamazaki, Chie Furuta, Ryutaro Hirasawa, Yohei Morita, Mitsujiro Osawa, Tsutomu Motohashi, Koji Eto, Hideo Ema, Toshio Kitamura, Dietmar Vestweber, and Hiromitsu Nakauchi

1493 HIF-1–dependent repression of equilibrative nucleoside transporter (ENT) in hypoxia
Holger K. Eltzschig, Parween Abdulla, Edgar Hoffman, Kathryn E. Hamilton, Dionne Daniels, Caroline Schönfeld, Michaela Löffler, German Reyes, Michael Duszenko, Jorn Karhausen, Andreas Robinson, Karen Westerman, Imogen R. Coe, and Sean P. Colgan
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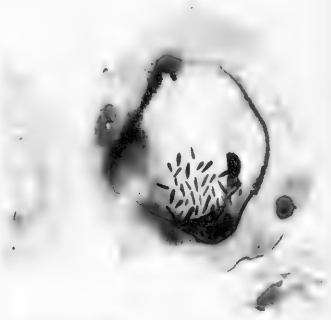

ON THE COVER
Painting by New York artist Emilie Clark (emilie@sharkbooks.com). Image shows a T lymphocyte lacking the tyrosine phosphatase MEG2. These cells fail to form mature secretory vesicles and become clogged with abnormal dense particles. Related article by Wang et al.
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1507 **Innate NKT lymphocytes confer superior adaptive immunity via tumor-capturing dendritic cells**
Kang Liu, Juliana Idoyaga, Anna Charalambous, Shin-ichiro Fujii, Anthony Bonito, Jose Mordoh, Rosa Wainstok, Xue-Feng Bai, Yang Liu, and Ralph M. Steinman

1517 **Structural basis for CD1d presentation of a sulfatide derived from myelin and its implications for autoimmunity**
Dirk M. Zajonc, Igor Maricic, Douglass Wu, Ramesh Halder, Keshab Roy, Chi-Huey Wong, Vipin Kumar, and Ian A. Wilson

1527 **A fundamental bimodal role for neuropeptide Y1 receptor in the immune system**
Julie Wheway, Charles R. Mackay, Rebecca A. Newton, Amanda Sainsbury, Dana Boey, Herbert Herzog, and Fabienne Mackay
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1539 **Resolution of airway inflammation and hyperreactivity after in vivo transfer of $CD4^+CD25^+$ regulatory T cells is interleukin 10 dependent**
Jennifer Kearley, Jane E. Barker, Douglas S. Robinson, and Clare M. Lloyd
See commentary on page 1459

1549 **$CD4^+CD25^+$ T cells protect against experimentally induced asthma and alter pulmonary dendritic cell phenotype and function**
Ian P. Lewkowich, Nancy S. Herman, Kathleen W. Schleifer, Matthew P. Dance, Brian L. Chen, Krista M. Dienger, Alyssa A. Sproles, Jaimin S. Shah, Jörg Köhl, Yasmine Belkaid, and Marsha Wills-Karp
See commentary on page 1459

1563 **Immunostimulatory oligonucleotides block allergic airway inflammation by inhibiting Th2 cell activation and IgE-mediated cytokine induction**
Edith M. Hessel, Mabel Chu, Jennifer O. Lizcano, Bonnie Chang, Nancy Herman, Sariah A. Kell, Marsha Wills-Karp, and Robert L. Coffman
See news item on page 1457

1575 **Immune stimulation mediated by autoantigen binding sites within small nuclear RNAs involves Toll-like receptors 7 and 8**
Jörg Vollmer, Sibylle Tluk, Claudia Schmitz, Svetlana Hamm, Marion Jurk, Alexandra Forsbach, Shizuo Akira, Kindra M. Kelly, Westley H. Reeves, Stefan Bauer, and Arthur M. Krieg
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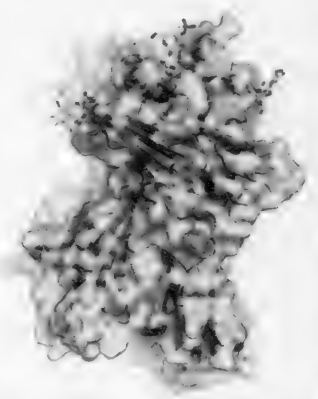

**Mouse CD1d molecules (grey) bind the glycolipid sulfatide such that its carbohydrate headgroup (yellow) is exposed, allowing recognition by sulfatide-specific NKT cells.**
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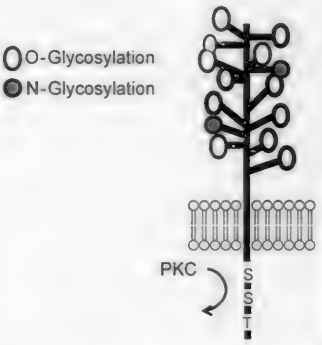


**Endomucin, an endothelial sialomucin, is a marker for long-term repopulating hematopoietic stem cells.**
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1587 **Tyrosine phosphatase MEG2 modulates murine development and platelet and lymphocyte activation through secretory vesicle function**
Yingchun Wang, Eric Vachon, Jinyi Zhang, Vera Cherepanov, Joshua Kruger, Jun Li, Kan Saito, Patrick Shannon, Nunzio Bottini, Huong Huynh, Heyu Ni, Hong Yang, Colin McKerlie, Sue Quaggin, Zhizhuang Joe Zhao, Philip A. Marsden, Tomas Mustelin, Katherine A. Siminovitch, and Gregory P. Downey
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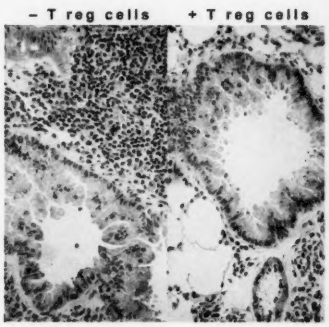
1599 **Global analysis of proliferation and cell cycle gene expression in the regulation of hematopoietic stem and progenitor cell fates**
Emmanuelle Passegué, Amy J. Wagers, Sylvie Giuriato, Wade C. Anderson, and Irving L. Weissman




**Inhibition of allergic airway inflammation by allergen-specific regulatory T cells requires interleukin-10.**
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1614 How SLPI soothes
Chemokine drives tuberculosis
New hope for tumor vaccines
A toxic gas eases IBD
Heather Van Epps

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1617 Tuberculosis in children and adults: two distinct genetic diseases
Alexandre Alcaïs, Claire Fieschi, Laurent Abel, and Jean-Laurent Casanova

1623 Functionally distinct NKT cell subsets and subtypes
Ken-ichiro Seino and Masaru Taniguchi

## BRIEF DEFINITIVE REPORTS

1627 A nonclassical non-Vα14Jα18 CD1d-restricted (type II) NKT cell is sufficient for down-regulation of tumor immunosurveillance
Masaki Terabe, Jeremy Swann, Elena Ambrosino, Pratima Sinha, Shun Takaku, Yoshihiro Hayakawa, Dale I. Godfrey, Suzanne Ostrand-Rosenberg, Mark J. Smyth, and Jay A. Berzofsky
See commentary on page 1623

1635 Mastocytosis in mice expressing human Kit receptor with the activating Asp816Val mutation
Jacques P. Zappulla, Patrice Dubreuil, Sabine Desbois, Sébastien Létard, Nadine Ben Hamouda, Marc Daëron, Georges Delsol, Michel Arock, and Roland S. Liblau

1643 Hydronephrosis associated with antiurothelial and antinuclear autoantibodies in BALB/c-*Fcgr2b*$^{-/-}$*Pdcd1*$^{-/-}$ mice
Taku Okazaki, Yumi Otaka, Jian Wang, Hiroshi Hiai, Toshiyuki Takai, Jeffrey V. Ravetch, and Tasuku Honjo

## ARTICLES

1649 A functional promoter polymorphism in *monocyte chemoattractant protein–1* is associated with increased susceptibility to pulmonary tuberculosis
Pedro O. Flores-Villanueva, Jorge A. Ruiz-Morales, Chang-Hwa Song, Ludmila M. Flores, Eun-Kyeng Jo, Marta Montaño, Peter F. Barnes, Moises Selman, and Julio Granados
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JEM
THE JOURNAL OF EXPERIMENTAL MEDICINE
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ON THE COVER
Image represents the cloudy appearance of the lungs typically seen in chest radiographs of patients with tuberculosis. A population study reveals that adults with a polymorphism in the *MCP1* gene, which results in increased production of the chemokine MCP-1 are more susceptible to developing active tuberculosis. Related article by Flores-Villanueva et al.
See page 1649

1659 **Secretory leucoprotease inhibitor binds to NF-κB binding sites in monocytes and inhibits p65 binding**
Clifford C. Taggart, Sally-Ann Cryan, Sinead Weldon, Aileen Gibbons, Catherine M. Greene, Emer Kelly, Teck Boon Low, Shane J. O'Neill, and Noel G. McElvaney
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1669 **E47 is required for V(D)J recombinase activity in common lymphoid progenitors**
Lisa Borghesi, Jennifer Aites, Shakira Nelson, Preslav Lefterov, Pamela James, and Rachel Gerstein

1679 **Suppression of tumor formation in lymph nodes by L-selectin–mediated natural killer cell recruitment**
Shihao Chen, Hiroto Kawashima, John B. Lowe, Lewis L. Lanier, and Minoru Fukuda

1691 **Caspase-dependent immunogenicity of doxorubicin-induced tumor cell death**
Noelia Casares, Marie O. Pequignot, Antoine Tesniere, François Ghiringhelli, Stéphan Roux, Nathalie Chaput, Elise Schmitt, Ahmed Hamai, Sandra Hervas-Stubbs, Michel Obeid, Frédéric Coutant, Didier Métivier, Evelyne Pichard, Pierre Aucouturier, Gérard Pierron, Carmen Garrido, Laurence Zitvogel, and Guido Kroemer
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1703 **Carbon monoxide ameliorates chronic murine colitis through a heme oxygenase 1–dependent pathway**
Refaat A.F. Hegazi, Kavitha N. Rao, Aqila Mayle, Antonia R. Sepulveda, Leo E. Otterbein, and Scott E. Plevy
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1715 **TLR9 regulates Th1 responses and cooperates with TLR2 in mediating optimal resistance to *Mycobacterium tuberculosis***
Andre Bafica, Charles A. Scanga, Carl G. Feng, Cynthia Leifer, Allen Cheever, and Alan Sher

**Deletion of the inhibitory receptors FcgRIIB and PD-1 in mice triggers hydronephrosis and the production of autoantibodies that bind to urothrial cells (green) in the bladder.**
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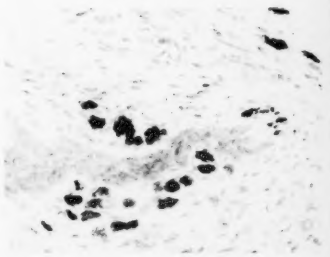

**Mice with a point mutation in the Kit protooncogene develop mastocytosis, which is characterized by the accumulation of mast cells (purple) in the skin (shown) as well as in other organs and tissues.**
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